General

Guideline Title

Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline.

Bibliographic Source(s)

Armenian SH, Lacchetti C, Barac A, Carver J, Constine LS, Denduluri N, Dent S, Douglas PS, Durand JB, Ewer M, Fabian C, Hudson M, Jessup M, Jones LW, Ky B, Mayer EL, Moslehi J, Oeffinger K, Ray K, Ruddy K, Lenihan D. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2017 Mar 10;35(8):893-911. [160 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the rating of evidence (High, Intermediate, Low, Insufficient); types of recommendations (Evidence based, Formal consensus, Informal consensus, No recommendation); and strength of recommendations (Strong, Moderate, Weak) are provided at the end of the "Major Recommendations" field.

Clinical Question 1

Which patients with cancer are at increased risk for developing cardiac dysfunction?

Recommendation 1.1

It is recommended that patients with cancer who meet any of the following criteria should be considered at increased risk for developing cardiac dysfunction.

- Treatment that includes any of the following:
  - High-dose anthracycline (e.g., doxorubicin ≥250 mg/m², epirubicin ≥600 mg/m²)
  - High-dose radiation therapy (RT) (≥30 Gy) where the heart is in the treatment field
  - Lower-dose anthracycline (e.g., doxorubicin <250 mg/m², epirubicin <600 mg/m²) in combination with lower-dose RT (<30 Gy) where the heart is in the treatment field
- Treatment with lower-dose anthracycline (e.g., doxorubicin <250mg/m², epirubicin <600mg/m²) or trastuzumab alone, and presence of any of the following risk factors:

    - Multiple cardiovascular risk factors (≥ two risk factors), including smoking, hypertension, diabetes, dyslipidemia, and obesity, during or after completion of therapy
    - Older age (≥60 years) at cancer treatment
    - Compromised cardiac function (e.g., borderline low left ventricular ejection fraction [LVEF] [50% to 55%], history of myocardial infarction, ≥ moderate valvular heart disease) at any time before or during treatment
- Treatment with lower-dose anthracycline (e.g., doxorubicin <250 mg/m², epirubicin <600 mg/m²) followed by trastuzumab (sequential therapy)

(type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate)

Recommendation 1.2

No recommendation can be made on the risk of cardiac dysfunction in patients with cancer with any of the following treatment exposures:

- Lower-dose anthracycline (e.g., doxorubicin <250 mg/m², epirubicin <600 mg/m²) or trastuzumab alone and no additional risk factors (as defined in Recommendation 1.1)
- Lower-dose RT (<30 Gy) where the heart is in the treatment field and no additional cardiotoxic therapeutic exposures or risk factors (as defined in Recommendation 1.1)
- Kinase inhibitors (KIs)

(type: evidence based; evidence quality: low)

Clinical Question 2

Which preventative strategies minimize risk before initiation of therapy?

Recommendation 2.1

Avoid or minimize the use of potentially cardiotoxic therapies if established alternatives exist that would not compromise cancer-specific outcomes (type: consensus based; benefits outweigh harms; strength of recommendation: strong).

Recommendation 2.2

Clinicians should perform a comprehensive assessment in patients with cancer that includes a history and physical examination, screening for cardiovascular disease risk factors (hypertension, diabetes, dyslipidemia, obesity, smoking), and an echocardiogram before initiation of potentially cardiotoxic therapies (type: evidence and consensus based; benefits outweigh harms; evidence quality: high; strength of recommendation: strong).

Clinical Question 3

Which preventive strategies are effective in minimizing risk during the administration of potentially cardiotoxic cancer therapy?

Recommendation 3.1

Clinicians should screen for and actively manage modifiable cardiovascular risk factors (e.g., smoking, hypertension, diabetes, dyslipidemia, obesity) in all patients receiving potentially cardiotoxic treatments (type: informal consensus and evidence based; benefits outweigh harms; evidence quality: insufficient; strength of recommendation: moderate).

Recommendation 3.2

Clinicians may incorporate a number of strategies, including use of the cardioprotectant dexrazoxane, continuous infusion, or liposomal formulation of doxorubicin, for prevention of cardiotoxicity in patients planning to receive high-dose anthracyclines (e.g., doxorubicin ≥250 mg/m², epirubicin ≥600 mg/m²) (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Recommendation 3.3

For patients who require mediastinal RT that might impact cardiac function, clinicians should select lower radiation doses when clinically appropriate and use more precise or tailored radiation fields with exclusion of as much of the heart as possible. These goals can be accomplished through use of advanced techniques including the following:

- Deep-inspiration breath holding for patients with mediastinal tumors or breast cancer in which the heart might be exposed
- Intensity-modulated RT that varies the radiation energy while treatment is delivered to precisely contour the desired radiation distribution

and avoid normal tissues

(type: evidence based and informal consensus; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: strong)

Clinical Question 4

What are the preferred surveillance and monitoring approaches during treatment in patients at risk for cardiac dysfunction?

Recommendation 4.1

Clinicians should complete a careful history and physical examination in patients who are receiving potentially cardiotoxic treatments (type: informal consensus; benefits outweigh harms; evidence quality: insufficient; strength of recommendation: strong).

Recommendation 4.2

In individuals with clinical signs or symptoms concerning for cardiac dysfunction during routine clinical assessment, the following strategy is recommended:

- Echocardiogram for diagnostic workup (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: strong)
- Cardiac magnetic resonance imaging (MRI) or multigated acquisition (MUGA) if echocardiogram is not available or technically feasible (e.g., poor image quality), with preference given to cardiac MRI (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate)
- Serum cardiac biomarkers (troponins, natriuretic peptides) or echocardiography-derived strain imaging in conjunction with routine diagnostic imaging (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate)
- Referral to a cardiologist based on findings (type: informal consensus; benefits outweigh harms; evidence quality: insufficient; strength of recommendation: strong)

Recommendation 4.3

Routine surveillance imaging may be offered during treatment in asymptomatic patients considered to be at increased risk (Recommendation 1.1) of developing cardiac dysfunction. In these individuals, echocardiography is the surveillance imaging modality of choice that should be offered. Frequency of surveillance should be determined by health care providers based on clinical judgment and patient circumstances (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Recommendation 4.4

No recommendations can be made regarding continuation or discontinuation of cancer therapy in individuals with evidence of cardiac dysfunction. This decision, made by the oncologist, should be informed by close collaboration with a cardiologist, fully evaluating the clinical circumstances and considering the risks and benefits of continuation of therapy responsible for the cardiac dysfunction (type: informal consensus; benefits outweigh harms; evidence quality: insufficient).

Recommendation 4.5

Clinicians may use routine echocardiographic surveillance in patients with metastatic breast cancer continuing to receiving trastuzumab indefinitely. The frequency of cardiac imaging for each patient should be determined by health care providers based on clinical judgment and patient circumstances (type: evidence based and informal consensus; benefits outweigh harms; evidence quality: low; strength of recommendation: moderate).

Clinical Question 5

What are the preferred surveillance and monitoring approaches after treatment in patients at risk for cardiac dysfunction?

Recommendation 5.1

Clinicians should complete a careful history and physical examination in survivors of cancer previously treated with potentially cardiotoxic therapies (type: informal consensus; benefits outweigh harms; evidence quality: insufficient; strength of recommendation: strong).

Recommendation 5.1.1

In individuals with clinical signs or symptoms concerning for cardiac dysfunction, the following approaches should be offered as part of recommended care:

- Echocardiogram for diagnostic workup (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: strong)
- Cardiac MRI or MUGA if echocardiogram is not available or technically feasible (e.g., poor image quality), with preference given to cardiac MRI (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate)
- Serum cardiac biomarkers (troponins, natriuretic peptides) (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate)
- Referral to a cardiologist based on findings (type: informal consensus; benefits outweigh harms; evidence quality: insufficient; strength of recommendation: strong)

Recommendation 5.2

An echocardiogram may be performed between 6 and 12 months after completion of cancer-directed therapy in asymptomatic patients considered to be at increased risk (Recommendation 1.1) of cardiac dysfunction (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Recommendation 5.2.1

Cardiac MRI or MUGA may be offered for surveillance in asymptomatic individuals if an echocardiogram is not available or technically feasible (e.g., poor image quality), with preference given to cardiac MRI (type: evidence based; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Recommendation 5.3

Patients identified to have asymptomatic cardiac dysfunction during routine surveillance should be referred to a cardiologist or a health care provider with cardio-oncology expertise for further assessment and management (type: informal consensus; benefits outweigh harms; evidence quality: insufficient; strength of recommendation: strong).

Recommendation 5.4

No recommendations can be made regarding the frequency and duration of surveillance in patients at increased risk (Recommendation 1.1) who are asymptomatic and have no evidence of cardiac dysfunction on their 6- to 12-month post-treatment echocardiogram (type: informal consensus; relative balance of benefits and harms; evidence quality: insufficient).

Recommendation 5.5

Clinicians should regularly evaluate and manage cardiovascular risk factors such as smoking, hypertension, diabetes, dyslipidemia, and obesity in patients previously treated with cardiotoxic cancer therapies. A heart-healthy lifestyle, including the role of diet and exercise, should be discussed as part of long-term follow-up care (type: evidence based and consensus; benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Definitions

Guide for Rating Strength of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal Consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Cancer
- Treatment-related cardiac dysfunction (cardiotoxicity)

Guideline Category

Evaluation

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Cardiology

Family Practice

Internal Medicine

Oncology

Radiation Oncology

Intended Users

Advanced Practice Nurses

Patients

Physician Assistants

Physicians

Guideline Objective(s)

To develop recommendations for prevention and monitoring of cardiac dysfunction in survivors of adult-onset cancers

Target Population

Adults with cancer for whom cardiotoxic anticancer therapies are being considered

Interventions and Practices Considered

1. Risk factor assessment for development of treatment-related cardiac dysfunction
    - Assessment of anthracycline use and dose
    - Assessment of radiation usage and dose
    - Assessment of pre-existing cardiovascular risk factors
2. Preventive strategies for minimizing risk before treatment initiation
    - Avoiding or minimizing the use of potentially cardiotoxic therapies
    - Comprehensive assessment including a history and physical examination, screening for cardiovascular disease risk factors, and an echocardiogram before initiation of potentially cardiotoxic therapies
3. Preventive strategies for minimizing risk during treatment administration
    - Screening for and actively managing modifiable cardiovascular risk factors
    - Use of dexrazoxane, or continuous infusion or liposomal formulation of doxorubicin
    - Use of lower radiation doses and exclusion of the heart from the radiation field
4. Surveillance/monitoring approaches during cardiotoxic treatment
    - History and examination
    - Echocardiogram

- Cardiac magnetic resonance imaging (MRI)
- Multigated acquisition (MUGA)
- Serum cardiac biomarkers (troponins, natriuretic peptides) or echocardiography-derived strain imaging
- Referral to cardiologist
- Routine echocardiographic surveillance in patients with metastatic breast cancer continuing to receiving trastuzumab indefinitely

5. Surveillance/monitoring approaches after treatment
    - Echocardiogram
    - Cardiac MRI or MUGA
    - Serum cardiac biomarkers (troponins, natriuretic peptides)
    - Referral to a cardiologist
    - Regular evaluation and management of cardiovascular risk factors

Note: The following were considered but no recommendations were made: assessment of kinase inhibitor use, continuation/discontinuation of cancer therapy in individuals with evidence of cardiac dysfunction, frequency and duration of surveillance in patients at increased risk.

Major Outcomes Considered

- Asymptomatic or symptomatic cardiac dysfunction
- Cancer-specific outcomes
- Utility and accuracy of surveillance with cardiac imaging (e.g., echocardiography, strain, tissue Doppler, magnetic resonance imaging [MRI], multigated acquisition [MUGA] scan) or blood-based biomarkers for detection of cardiac dysfunction
- Effectiveness of interventions in asymptomatic cancer survivors for prevention of symptomatic disease

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Literature Review and Strategy

American Society of Clinical Oncology (ASCO) guidelines are based on systematic reviews. A protocol for each guideline defines the parameters for a targeted literature search including relevant study designs, literature sources, types of reports, and prespecified study selection criteria for identified literature. For this guideline, the MEDLINE (Ovid: 1996 through May [week 2] 2014) database was searched for evidence reporting on outcomes of interest. An updated literature search (period: May 2014 to February 16, 2016) was conducted in PubMed to identify relevant studies that may impact the current recommendations. Reference lists from seminal articles and recent review articles were scanned for additional citations, and known updates of included evidence were obtained as available. The literature search strategy used in the MEDLINE and PubMed databases is available in the Data Supplement (see the "Availability of Companion Documents" field).

Study Selection Criteria

Articles were eligible for inclusion in this review of the evidence if they met the following criteria.

Question 1. Risk Categorization

- Population-based cohort studies with long-term and complete follow-up that included validated cardiovascular outcomes, treatment dose–specific information, comparison with no exposure, and multivariable regression analysis that adjusted for confounders.

Question 2. Prevention before Initiation of Cancer-Directed Treatment

- Comparative studies that considered prevention strategies of interest.

Question 3. Prevention during Cancer-Directed Treatment

- Studies that considered prevention strategies of interest, including limitation of cardiotoxic antineoplastic dose or exposure, alternative drug administration schedules, use of less cardiotoxic analogs, limitation of total radiation therapy (RT) dose, precision of RT volume to avoid heart, use of cardioprotectants, and management of modifiable risk factors.
- Results were reported for development of asymptomatic or symptomatic cardiac dysfunction.

Question 4. Surveillance during Treatment

- Studies that described the incidence of cardiac dysfunction (asymptomatic or symptomatic) as a result of specific therapeutic exposures during treatment.
- Comparative studies that evaluated the utility and accuracy of surveillance with cardiac imaging (e.g., echocardiography, strain, tissue Doppler, magnetic resonance imaging [MRI], multigated acquisition [MUGA] scan) or blood-based biomarkers for detection of cardiac dysfunction.

Question 5. Surveillance after Treatment

- Studies describing the incidence of asymptomatic or symptomatic cardiac dysfunction over time were collected to inform the frequency and duration of long-term surveillance.
- Comparative studies that evaluated the utility and accuracy of surveillance with cardiac imaging (e.g., echocardiography, strain, tissue Doppler, MRI, MUGA) or blood-based biomarkers for detection of cardiac dysfunction.
- Studies that examined the effectiveness of interventions in asymptomatic cancer survivors for prevention of symptomatic disease.

Articles were excluded from the systematic review if they were editorials, commentaries, letters, news articles, case reports, or narrative reviews; published in a non-English language; or described studies that included fewer than 20 participants. Meeting abstracts not yet published in peer-reviewed journals were generally excluded for review, except when there was uniform consensus from the Expert Panel regarding their importance for the formulation of recommendations.

Number of Source Documents

Study quality was formally assessed for 104 studies. A total of eight systematic reviews, 12 randomized controlled trials (RCTs), 49 cohort studies, 32 before-and-after studies, and three cross-sectional studies met eligibility criteria and form the evidentiary basis for the guideline recommendations.

See Data Supplement 3 (see the "Availability of Companion Documents" field) for a Quality of Reporting of Meta-analyses (QUOROM) Diagram showing exclusions and inclusions of publications identified for the systematic review.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Guide for Rating Strength of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.

Rating for Strength of Evidence	Definition
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.
Insufficient Evidence	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Rating of Potential for Bias

Rating of Potential for Bias	Definitions for Rating Potential for Risk of Bias in Randomized Controlled Trials
Low risk	No major features in the study that risk biased results, and none of the limitations are thought to decrease the validity of the conclusions. The study avoids problems such as failure to apply true randomization, selection of a population unrepresentative of the target patients, high dropout rates, and no intention-to-treat analysis; and key study features are described clearly (including the population, setting, interventions, comparison groups, measurement of outcomes, and reasons for dropouts).
Intermediate	The study is susceptible to some bias, but flaws are not sufficient to invalidate the results. Enough of the items introduce some uncertainty about the validity of the conclusions. The study does not meet all the criteria required for a rating of good quality, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
High risk	There are significant flaws that imply biases of various types that may invalidate the results. Several of the items introduce serious uncertainty about the validity of the conclusions. The study has serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Study Quality Assessment

Systematic reviews and meta-analyses were assessed for quality using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) tool. Design elements, such as blinding, allocation concealment, placebo control, intention to treat, and funding sources, were assessed for randomized controlled trials (RCTs). Methodologic criteria assessed for cohort studies and before-and-after studies included type of data collection, sampling method, representativeness of participants, objective outcomes, and appropriate statistical analyses. Assessment of cross-sectional studies was informed by the Modified Newcastle-Ottawa Scale. The risk of bias for all included studies is assessed as "low," "intermediate," or "high". Ratings are described further in the "Rating Scheme for the Strength of the Evidence" field.

Data Extraction

Literature search results were reviewed and deemed appropriate for full-text review by an American Society of Clinical Oncology (ASCO) staff member in consultation with the co-chairs. Data were extracted by one ASCO staff member and subsequently checked for accuracy through an audit of the data by another ASCO staff member. Disagreements were resolved through discussion and consultation with the co-chairs if necessary. Evidence tables are provided in the Data Supplement (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition

The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPGC) convened an Expert Panel with multidisciplinary representation in medical oncology, radiation oncology, cardiology, exercise physiology, family medicine, cancer prevention, cancer survivorship, patient/advocacy representation, and guideline implementation. The Expert Panel was led by two Co-Chairs who had primary responsibility for the development and timely completion of the guideline. For this guideline product, the Co-Chairs selected additional members from the Update Committee to form a Writing Group/Steering Committee to assist in the development and review of the guideline drafts. The Expert Panel included representatives from the American College of Cardiology (ACC) and the American Heart Association (AHA).

Guideline Development Process

The Expert Panel met (in person/webinar) on several occasions and corresponded frequently through e-mail; progress on guideline development was driven primarily by the Co-Chairs/Writing Group/Steering Committee along with ASCO staff. The purpose of the meetings was for members to contribute content, provide critical review, interpret evidence, and finalize the guideline recommendations based upon the consideration of the evidence. All members of the Expert Panel participated in the preparation of the draft guideline document.

The guideline recommendations were crafted, in part, using the GuideLines Into DEcision Support (GLIDES) methodology. This method helps guideline panels systematically develop clear, translatable, and implementable recommendations using natural language, based on the evidence and assessment of its quality to increase usability for end users. The process incorporates distilling the actions involved, identifying who will carry them out, to whom, under what circumstances, and clarifying if and how end users can carry out the actions consistently. This process helps the Panel focus the discussion, avoid using unnecessary and/or ambiguous language, and clearly state its intentions.

The recommendations were informed by a systematic review (1996 to 2016) of randomized clinical trials (RCTs), observational studies, and clinical experience. Where evidence was lacking but there was a high level of agreement among the panel members (>80% of panelists), informal consensus was used, as noted with the recommendations.

Rating Scheme for the Strength of the Recommendations

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal Consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the

Rating for Strength of Recommendation	Definition
	guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Members of the Expert Panel were responsible for reviewing and approving the penultimate version of the guideline. All American Society of Clinical Oncology (ASCO) guidelines are ultimately reviewed and approved by the ASCO Clinical Practice Guideline Committee before publication. The guideline also underwent formal review by the American College of Cardiology (ACC) and the American Heart Association (AHA) and was approved for endorsement by both organizations.

External Review

The draft of this guideline was submitted to two ASCO external reviewers with content expertise. It was rated as high quality, and it was agreed that it would be useful in practice. In addition, the guideline was reviewed by two peer reviewers from the ACC and two reviewers from the AHA, as well as the AHA Science Advisory and Coordinating Committee. Their comments were reviewed by the Expert Panel and integrated into the final article before approval by the ASCO Clinical Practice Guideline Committee (CPGC).

The CPGC approved this guideline on June 13, 2016.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Cardiac dysfunction is a serious adverse effect of certain cancer-directed therapies that can interfere with the efficacy of treatment, decrease quality of life, or impact the actual survival of the patient with cancer. Screening guidelines in survivors of adult-onset cancers is paramount, so that proper interventions can be implemented to avert the risk of cardiac dysfunction during and after completion of therapy.
- Certain higher risk populations of survivors of cancer may benefit from prevention and screening strategies implemented during cancer-directed therapies.

Refer to the "Literature review and clinical interpretation" sections of the original guideline document for a detailed discussion of the potential benefits and harms of each recommendation.

Potential Harms

Although there is potential value to early diagnosis and treatment of cardiac dysfunction, it is important to note that screening for asymptomatic cardiac dysfunction using advanced imaging might lead to added distress in survivors of cancer. This may be especially true in survivors of cancer in whom the prevalence of cardiac dysfunction is expected to be low, because the positive predictive value of the screening test will be low as well.

Refer to the "Literature review and clinical interpretation" sections of the original guideline document for a detailed discussion of the potential benefits and harms of each recommendation.

Qualifying Statements

Qualifying Statements

- The clinical practice guidelines and other guidance published herein are provided by American Society of Clinical Oncology (ASCO) to assist providers in clinical decision making. The information herein should not be relied on as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Furthermore, the information is not intended to substitute for the independent professional judgment of the treating provider, because the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of such words as "must," "must not," "should," and "should not" indicates that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in individual cases. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an as is basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.
- See the "Health Disparities" and "Multiple Chronic Conditions" sections in the original guideline document for additional qualifying information.
- See also the original guideline document for qualifying statements related to each recommendation.

Implementation of the Guideline

Description of Implementation Strategy

Guideline Implementation

American Society of Clinical Oncology (ASCO) guidelines are developed for implementation across health settings. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers, and also to provide adequate services in the face of limited resources. The guideline Bottom Line Box was designed to facilitate implementation of recommendations. This guideline will be distributed widely through the ASCO Practice Guideline Implementation Network. ASCO guidelines are posted on the ASCO Web site and most often published in *Journal of Clinical Oncology* and *Journal of Oncology Practice*.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate.

For additional information on the ASCO implementation strategy, please see the ASCO Web site .

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

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Guideline Committee

Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers Guideline Expert Panel

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Financial Disclosures/Conflicts of Interest

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the American Society of Clinical Oncology's (ASCO's) Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http://www.asco.org/rwc). All members of the panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria; consulting or advisory role; speakers' bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the panel did not disclose any relationships constituting a conflict under the Policy.

Authors' Disclosures and Potential Conflicts of Interest

The following represents disclosure information provided by authors of the guideline. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or jco.ascopubs.org/site/ifc .

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Guideline Endorser(s)

American College of Cardiology Foundation - Medical Specialty Society

American Heart Association - Professional Association

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of Clinical Oncology Web site.

Availability of Companion Documents

The following are available:

- Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. Methodology supplement. Alexandria (VA): American Society of Clinical Oncology; 2017. 18 p. Available from the Journal of Clinical Oncology Web site.
- Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. Data supplements 1-3. Alexandria (VA): American Society of Clinical Oncology; 2017. 48 p. Available from the Journal of Clinical Oncology Web site.
- Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2017. 24 p. Available in PDF and PowerPoint from the American Society of Clinical Oncology (ASCO) Web site.
- Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. Summary of recommendations table. Alexandria (VA): American Society of Clinical Oncology; 2017. 6 p. Available from the ASCO Web site.
- Armenian S, Lacchetti C, Lenihan D. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline summary. J Oncol Pract. 2017 Apr; 13(4):270-5. Available from the Journal of Oncology Practice Web site.

Patient Resources

Patient information about heart problems related to cancer treatment is available from the Cancer.Net Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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